UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FILE

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: August 4, 1998

SUBJECT: *ID#98 CA 0029.* SECTION 18 EXEMPTION FOR THE USE OF **Myclobutanil** ON **Artichokes** IN **California**.

DP Barcode:247019
Submission #:543754
Chemical#:128857
Trade Name: Rally 40W
EPA Reg#:707-215

PRAT Case#:290210
Caswell#:723K
Class: Fungicide
40 CFR:180.443

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INTRODUCTION

The **State of California Department of Pesticide Regulation (DPR)** is requesting a **specific exemption** for the use of **myclobutanil** on **artichokes** for control of **powdery mildew** (***Leveillula taurica***). Rohm and Haas Company, the registrant, has been notified of this specific exemption request and is in concurrence, and makes reference to the Notice of Filing (NOF) and to IR-4 petitions for the use of myclobutanil on artichokes. This is **the first** §18 request for this use in the state of California. ***In addition,*** *DPR requests that the U.S. EPA establish* ***a time- limited tolerance for artichokes treated with this product.*** Using the data provided by Rohm and Haas Company, the appropriate **time-limited tolerance would be 1.0 ppm**. The proposed program will entail application of: **1) aerial** = 35,000 gallons of **Rally 40W [4,200 lbs ai/acre/season];** or **2) Ground** = 525,000 gallons of **Rally 40W [4,200 lbs ai/acre/season]** on **7,000** acres, during the period **June 30, 1998 thru June 30, 1999 (or one year from issuance)**.

SUMMARY

Occupational exposure and aggregate risk estimates **do not** exceed HED's level of concern. This Section 18 exemption should not pose an unacceptable aggregate risk to infants, children, or adults. Therefore, HED **has no objection** to the issuance of this Section 18 exemption for the use of **myclobutanil** on **artichokes** in the State of **California**. A time-limited tolerance for residues of **myclobutanil and its metabolite alpha-(3-hydroxybutyl)-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile (free and bound)** in/on **artichokes** at 1.0

ppm should be established to support this Section 18 exemption.

TOXICOLOGICAL ENDPOINTS

DIETARY

1. *Acute Toxicity*

   None. For acute dietary risk assessment, the Hazard ID Assessment Review Committee (HIARC) did not recommend an acute dietary endpoint.

2. *Chronic Toxicity*

   RfD = 0.025 mg/kg/day. The RfD is currently established to be 0.025 mg/kg/day based on the NOEL from the chronic feeding study in the rat (2.49 mg/kg/day; MRID #00165247) and a safety factor of 100 [10 for intraspecies and 10 for interspecies]. The LOEL for the chronic rat feeding study is 9.84 mg/kg/day based on decreased testicular weight and increased testicular atrophy. The HIARC noted that the dose of 2.49 mg/kg/day established in the above study is supported by the Parental Systemic Toxicity NOEL and LOEL established in the Two-Generation reproduction study in rats. In that study the NOEL was 2.5 mg/kg/day and the LOEL was 10 mg/kg/day. The Committee determined that the **10 x** factor to account for enhanced sensitivity of infants and children (as required by FQPA) should be removed. A UF of 100 is adequate because of the following:

   (i) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

   (ii) A two generation reproduction toxicity study in rats showed no increased sensitivity in pups that were compared to adults.

   (iii) The toxicology data base is complete and there are no data gaps.

   This decision was confirmed by the *ad hoc* FQPA Safety Factor Committee (R. Keigwin and W. Burnam, personal communication). The Joint Meeting on Pesticide Residues (JMPR) established an ADI (RfD) of 0.03 mg/kg/day.

NON-DIETARY

1. *Short-Term Toxicity*

   For short-term Margin of Exposure (MOE) calculations, the HIARC recommended use of the systemic NOEL of 100 mg/kg/day [HDT] from the 28-day dermal toxicity study in rats (MRID# 266080). There was no LEL in the study.

2. *Intermediate-Term Toxicity*

   For intermediate-term MOE calculations, the HIARC recommended use of the reproductive NOEL of 10 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborns and a decrease in pup weight gain during lactation at the LOEL of 50 mg/kg/day (LOEL) from the 2-generation reproduction study in rats (MRID# 00143766, 00149581).

3. *Chronic Toxicity*

The HIARC determined that a chronic toxicity endpoint and risk assessment for myclobutanil is not required for workers.

4. *Dermal Penetration*

For short-term MOE calculations, a dermal toxicity study was used, so dermal penetration data were not required. The HIARC determined that a dermal absorption factor of 100% should be used for risk assessment because 1) a dermal absorption study was not available with the technical and 2) a dermal absorption factor could not be estimated due to the lack of comparative NOELs/LOELs from oral and dermal toxicity studies in the same species with the technical. The dermal absorption factor is required for Intermediate and Long-Term dermal risk assessment since oral doses were selected for these exposure periods. Dermal absorption is not required for Short-Term dermal exposure risk assessment since a dermal dose from a 28-day dermal toxicity study was selected for this time period.

CANCER

Myclobutanil is classified as Category E: not carcinogenic in two acceptable animal studies. Q_1^* is not applicable.

EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residues in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other outdoor and indoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. *From Food and Feed Uses:*

Tolerances have been established (40 CFR 180.443) for the residues of myclobutanil [alpha-butyl-]alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile] and its metabolite alpha-(3-hydroxybutyl)-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile (free and bound), expressed as myclobutanil, in or on a variety of raw agricultural commodities and processed commodities at levels ranging from 0.02 ppm in cottonseed to 25.0 ppm in raisin waste. Meat, milk, poultry and egg tolerances have been established at levels ranging from 0.02 ppm to 1.0 ppm.

Acute Risk. The HIARC did not recommend an acute dietary toxicological endpoint so an acute dietary risk assessment is not required (10/21/97 meeting).

Chronic Risk. In conducting this chronic dietary (food only) risk assessment, HED has made conservative assumptions. With the exceptions of selected commodities which were corrected for percent crop treated, all commodities having myclobutanil tolerances were assumed to contain myclobutanil and metabolite residues at the level of the established tolerance. This results in an overestimate of human dietary exposure. Thus, in making a safety determination for this tolerance, EPA is taking into account this partially refined exposure assessment.

The Dietary Exposure Evaluation Model (DEEM™) analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-91 nationwide Continuing Surveys for Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The chronic DEEM™ used mean consumption (3 day average) and gave the following results:

Subgroups	Exposure (mg/kg/day)	% RfD
U.S. Population (48 states)	0.005978	23.9
Non-Hispanic other than black or white	0.007454	29.8
All infants (< 1 year)	0.013618	54.5
Nursing Infants (< 1 year old)	0.005964	23.9
Non-Nursing Infants (< 1 year old)	0.016840	67.4
Children (1-6 years old)	0.018265	73.1
Children (7-12 years old)	0.008602	34.4
Females (13+/nursing)	0.007627	30.5

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and, (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

2. *From Drinking Water:*

Based on information in the EFED One Liner Database (updated: 12/20/94), myclobutanil is persistent and not considered mobile in soils with the exception of sandy soils. Data are not available for its metabolite alpha-(3-hydroxybutyl)-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile. There is no established Maximum Contaminant Level for residues of myclobutanil in drinking water (Safe Drinking Water Hotline - personal communication 5/14/97). No Health Advisory Levels for myclobutanil in drinking water have been established. The "Pesticides in Groundwater Database" (EPA 734-12-92-001, September 1992) has no information concerning myclobutanil.

The Environmental Fate and Effects Division (D239591, Douglas Urban, 11/4/97) has provided estimates of ground and surface water concentrations for myclobutanil based on the label rate of 0.65 lbs a.i./acre and assuming 15 applications per season. (The water numbers were based on turf.) The surface water numbers are based on the results of GENEEC model run. The ground water numbers are based on a screening tool, SCI-GROW, which tends to overestimate the true concentrations in the environment.

Surface water EEC [based on the results of a GENEEC (Version 1.2, 5/3/95) model run]
Acute = 145.96 ppb (0.14596 ppm or mg/L)(maximum initial concentration)
Chronic = 118.6 ppb (0.1186 ppm or mg/L)(average 56-day concentration)

NOTE: OPP policy allows the 90/56-day GENEEC value to be divided by 3 to obtain a value for chronic risk assessment calculations. Therefore, the surface water value for use in the chronic risk assessment would be 0.04 ppm or mg/L.

Ground water EEC (SCI-GROW, Lotus 1-2-3 spreadsheet)

3.6 ppb (0.0036 ppm or mg/L) (use for both acute and chronic)

Chronic exposure from surface water is calculated below. Chronic exposure from ground water is lower.

OPP has calculated drinking water levels of concern (DWLOCs) for chronic (non-cancer) exposure to be **0.7 ppm** for U.S. population, **0.6 ppm** for Non-Hispanic other than black or white, and **0.07 ppm** for Children (1-6 years old). To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DRES) was subtracted from the RfD to obtain the acceptable chronic (non-cancer) exposure to myclobutanil in drinking water.

Note: The following formula was used to convert maximum allowable water exposure to ppb. DWLOCs were then calculated using default body weights (70 kg - adult, 10 kg - child) and drinking water consumption figures (2 L - adult, 1 L child).

$$DWLOC\ (\mu g/L) = \frac{water\ exposure\ (mg/kg/day)\ x\ (body\ weight)}{consumption\ (L)\ x\ 10^{-3}\ mg/\mu g}$$

The estimated average concentration of myclobutanil in surface water is **0.04 ppm**. Chronic concentrations in ground water are not expected to be higher than the acute concentrations. The estimated average concentrations of myclobutanil in surface water are less than OPP's levels of concern for myclobutanil in drinking water as a contribution to chronic aggregate exposure. Therefore, taking into account the present uses and uses proposed in this action, OPP concludes with reasonable certainty that residues of myclobutanil in drinking water (when considered along with other sources of exposure for which OPP has reliable data) would not result in unacceptable levels of aggregate human health risk at this time.

OPP bases this determination on a comparison of estimated concentrations of myclobutanil in surface waters and ground waters to back-calculated "levels of concern" for myclobutanil in drinking water. These levels of concern in drinking water were determined after OPP has considered all other non-occupational human exposures for which it has reliable data, including all current uses, and uses considered in this action. The estimates of myclobutanil in surface waters are derived from water quality models that use conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface and ground water. Because OPP considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses are added in the future, OPP will reassess the potential impacts of myclobutanil on drinking water as a part of the aggregate risk assessment process.

3. *From Non-Dietary Uses:*

Myclobutanil is currently registered for outdoor residential and greenhouse use on annuals and perennials, turf, shrubs, trees, and flowers (Reference Files System/OPP LAN, date searched: 6/5/97). HED has determined that these uses do not constitute a chronic exposure scenario, but may constitute a short- to intermediate-term exposure scenario (**Note: the intermediate-term potential exposure would come from Post-application (dermal for adult; and dermal + ingestion of soil only, due to the persistence of the pesticide in soil, for toddlers**). Other intermediate-term exposure scenarios are unlikely as dissipation is strongly influenced by the growth of the grass which needs weekly mowing (more frequently in spring) and most dissipation studies on lawns show considerable tailing off of residues by day 3 or 4; thus, the expectation of significant residues is very unlikely.

Homeowner-use Products

End-use products containing the active ingredient, myclobutanil, are marketed for homeowner use. The homeowner use with the greatest potential for exposure takes the form of small scale lawn application (**other additional application uses are on roses, flowers, ornamental shrubs and trees**) of a soluble concentrate with a hose-end, backpack, or trigger bottle sprayer. Application of these products is recommended at two week intervals. Short-term (and not intermediate-term exposures, because of the amount of time it takes to mix, load, and apply this product) exposure is considered only. Short-term exposure, pre- and during application, will be considered an aggregate potential exposure: a summation of this exposure will include exposure levels for: the mixer + loader + applicator + Post-application on day zero (day of application). Short- and intermediate-term exposure will be considered during post-application (*Note:* Intermediate-term exposure is addressed only during post-application scenarios).

Handler Exposures and Assumptions

HED has determined that there is potential for exposures to applicators and handlers during usual homeowner use-patterns associated with myclobutanil. Based on the use patterns, three exposure scenarios with the greatest potential for exposure are considered: 1) loading and application of a soluble concentrate product by low pressure handwand sprayer (trigger bottle sprayer); 2) loading and application of a soluble concentrate product by backpack; and 3) loading and application of a soluble concentrate product by garden hose end sprayer.

Short-term dermal exposure assessments using the Pesticide Handlers Exposure Database (PHED) Version 1.1 surrogate data and baseline risk calculations for homeowners are presented in Table 1. Table 2 summarizes the caveats (e.g., data confidence) and parameters specific to each exposure scenario and corresponding risk assessment.

TABLE 1. Baseline Short-Term Exposure and Risk Assessments for Homeowner Use of Myclobutanil

Exposure Scenario	Baseline Dermal + Inhalation Unit Exposure (mg/lb ai)[a]	Maximum Application Rate (lb ai/acre)[b]	Maximum Acres/Day[c]	Total Daily Exposure (mg ai/day)[d]	Total Daily Dose (mg ai/kg/day)[e] BW = 60 kg	Short-Term MOE[f]
1. Load/Apply Soluble Concentrate Using Low Pressure Handwand	100.03 100.03 *(0.03)* [h]	0.63 1.7[g] 0.63	0.50 0.50 0.50	32 85[g] *(9.4X10^{-3})* [h]	1.0 1.9[g] *(1.6X10^{-4})* [h]	100 53[g] *(62000)* [i]
2. Load/Apply Soluble Concentrate Using Backpack	5.1 *(0.03)* [h]	0.63 0.63	0.50 0.50	1.6 *(9.4X10^{-3})* [h]	0.49 *(1.6X10^{-4})* [h]	200 *(62000)* [i]
3. Load/Apply Soluble Concentrate Using Garden Hose End Sprayer	30.01 *(0.01)* [h]	0.63 0.63	0.50 0.50	9.4 *(3.2X10^{-3})* [h]	0.62 *(5.3X10^{-5})* [h]	160 *(190000)* [i]

a Baseline unit exposure (dermal + inhalation), taken from PHED Version 1.1 data in the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments dated December 18, 1997, represents short pants, short sleeve shirt, no gloves, and open loading.
Note: that for some PHED data correction, factors were applied to arrive at the baseline scenario.

b Application rate comes from maximum rates found on the Myclobutanil labels.

c Daily acres treated values are from Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments dated December 18, 1997, estimates of acreage that could be treated in a single day for each exposure scenario of concern.

d Total Daily Exposure (mg ai/day) = Unit exposure (mg/lb ai) x Application Rate (lbs ai/acre) x Acres Treated.

e Total Daily Dose (mg/kg/day) = Daily(dermal+inhalation) Exposure (mg a.i./day) + Post-application exposure on day of application (= 28 mg a.i./day) /body weight (BW kg). See calculation for Post-application exposure below.

f Margin of Exposure (MOE) = NOEL (mg/kg/day)/Daily Dose (mg/kg/day); *NOEL = 100mg/kg/day; MOE for 60kg*

g Worst case day (based on label) of potential exposures = mixer/loader and application of lawn +roses+tree+flowers.

h Inhalation unit exposure only, taken from PHED Version 1.1 data in the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments dated December 18, 1997, represents short pants, short sleeve shirt, no gloves, and open loading. *For Total Daily Dose (mg/kg/day) = Daily(inhalation) Exposure (mg a.i./day)/body weight (BW kg).*

i Short-term, inhalation exposure only, *MOE based on a NOEL= 10 mg/kg/day.*

Table 2. Exposure Scenario Descriptions for Selected Residential Uses of Myclobutanil

Exposure Scenario (Number)	Data Source	Standard Assumption[a]	Comments
Mixer/Loader/Applicator Descriptors			
Load/Apply Soluble Concentrate Using Low Pressure Handwand (1)	PHED V1.1	0.50 Acres	**Baseline:** Low confidence (9-80 replicates of ABC grade data) for dermal exposure. Medium confidence (80 replicates of ABC grade data) for inhalation.
Load/Apply Soluble Concentrate Using Backpack (2)	PHED V1.1	0.50 Acres	**Baseline:** Low confidence (9-11 replicates of AB grade data) for dermal exposure. Low confidence (11 replicates of A grade data) for inhalation.
Load/Apply Soluble Concentrate Using Garden Hose End Sprayer (3)	PHED V1.1	0.50 Acres	**Baseline:** Low confidence (8 replicates of C and E grade data) for dermal exposure. Low confidence (8 replicates of C grade data) for inhalation. *Based on one study.*

[a] Standard Assumptions based on Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments dated December 18, 1997. Baseline dermal exposure is based on the worker wearing short pants, short sleeve shirt, and no gloves.

Formulas for determining daily (dermal+Inhalation)exposure and risk to handlers are as follows:

$$\textit{Daily Exposure (mg a.i./day)} =$$

$$\textit{Unit Exposure (mg/lb)} \times \textit{Use Rate (lb a.i./acre)} \times \textit{Maximum Area Treated (acres/day)}$$

$$\textit{Daily (Dermal + Inhalation; or Inhalation only) Dose (mg a.i./kg bw/day)} =$$

$$\frac{\textit{Daily Exposure (mg a.i./day)}}{\textit{Body Weight (kg)}}$$

$$\textit{Margin of Exposure (MOE)} =$$

$$\frac{\textit{NOEL (mg/kg/day)}}{\textit{Daily (Dermal + Inhalation; or Inhalation only) Dose (mg/kg/day)}}$$

The following are important assumptions used in the residential exposure assessments:

- For the short-term exposure assume exposed person's body weight is 60 kg; For the toddler (age 3) assume exposed body weight is 15 kg;
- Footnotes for Table 1 include other assumptions.

Homeowner Post-Application Exposures and Assumptions

The potential for post-application homeowner exposure exists. For example, potential exposures would be expected following applications to lawns and ornamental garden sites. There are no chemical-specific data to use in assessing these potential exposures; therefore, a range finder post-application exposure and risk assessment was performed (Table 3). The assessment uses typical transfer coefficients (Tc); for Adults = 10,000 cm^2/hr (high activity for 4 hrs, Tier II.) and for Toddlers = 8,700 cm^2/hr (for 2hrs. default tier I). It also utilizes dislodgeable foliar residues (DFR) derived from the application rate and an estimated 10 percent [less conservative than the default 20 percent (which is based on foliar wash), but still much more conservative than the California's roller method study of rate available as dislodgeable (which had an average of 1-2 % of rate available as DFR)]. EPA believes that exposures following soluble concentrate applications with a low pressure handwand to plants, such as lawn-turfgrass, are likely to represent a reasonably conservative post-application exposure estimate to homeowners and children. Total aggregate short-term exposure was calculated for adults and toddlers (for toddlers include dermal + incidental non-dietary ingestion (hand to mouth; surface area for one hand=175cm^2)). Isolated scenarios for short-term exposure for toddlers also include; ingestion of treated turfgrass, and ingestion of treated soil. Intermediate-term exposure for adults will be a mean value of a 14-day exposure scenario. For intermediate-term, total aggregate exposure for toddlers will include only, a mean value of a 14-day exposure scenario + the ingestion of soil. **Chemical-specific dissipation data and residential use/usage information are required to further refine these post-application exposure estimates.**

Table 3. Surrogate Post-application Range-Finder Assessment.

DAT[a]	DFR (µg/cm2)[b]	Dermal Dose (mg/kg/day)[c]		Adult Short-Term MOE[d]	Adult Intermediate-Term MOE[d]	Toddler Short-Term MOE[d]	Toddler Intermediate-Term MOE[d]
		BW = 60 kg	BW = 15 kg				
Exposure Activities (Tc = 10,000 cm^2/hr (adults-tier II); For toddlers 8,700 (default) cm^2/hr)[e]							
0	0.71	0.47[c1]	0.85[c2]	210[d1]	N/A	120[d2]	N/A
0	0.71	N/A	1.2 X10^{-3}[c3]	N/A	N/A	83,000[d3]	N/A
0	N/A	N/A	3.2 X10^{-5}[c4]	N/A	N/A	3.1 X10^{6}[d4]	N/A
0-14	0.71	0.04	N/A	N/A	250[d5]	N/A	N/A
0-14	0.71	N/A	6.1 X10^{-2}	N/A	N/A	N/A	160[d6]

a DAT is days after treatment based on an application rate of 1.44X10^{-5} lb ai/ ft^2.

b DFR (µg/cm^2) = Rate (lb ai/ft^2) x (weight conversion factor to convert the lbs a.i. in the application rate to µg for the DFR value = 4.54x 10^8 µg/lb) x (area unit conversion factor = 1.08 x 10^{-3} ft^2/cm^2) x percent (10 percent assumed) of rate available as dislodgeable

c **Dermal Dose** (mg/kg/day):c_1= *For Adult Females,*= **Dermal Dose** (mg/kg/day) = [DFR (µg/cm^2) x Tc (cm^2/hr) x (1 mg/1,000 µg unit conversion) x 4 hours/day(tier II)] / Body Weight (BW kg); c_2= *For Toddlers,*= **Dermal Dose** (mg/kg/day) = [DFR (µg/cm^2) x Tc (cm^2/hr) x (1 mg/1,000 µg unit conversion) x 2 hours/day(default) / Body Weight (BW kg) + **Incidental non-dietary ingestion of pesticide residues on residential lawns from hand to mouth transfer**=DFR X surface area of one hand (175 cm^2/event) X frequency of hand to mouth activity(1.56 events/hr) X exposure time (2hrs/day) X weight unit conversion factor (1 mg/1000 µg) / BW; *Isolated incidents for Toddlers, 1)* c_3= **Ingestion of treated turfgrass** = grass (and plant matter) residue on day of application (µg/cm^2) X ingestion rate of grass (25 cm^2/day) X conversion factor (mg/1000 µg) /BW; *and 2)* c_4 =, **Ingestion of treated soil** =soil residue on day of application (µg/g) X ingestion rate of soil (100 mg/day) X weight unit conversion factor (1 g/1X10^6 µg) / BW

d MOE = NOEL (mg/kg/day)/Dermal Dose (mg/kg/day); Short-term NOEL=100mg/kg/day and Intermediate-term NOEL=10mg/kg/day.d_1=*Short-term, Adult Females* ;d_2= *For Toddlers,* Short-term exposure, is an aggregate exposure scenario, which includes dermal+ incidental non-dietary ingestion hand to mouth. Other short-term exposure for toddlers, isolated incidents;d_3 = 1) ingestion of treated turf, & d_4 = 2) ingestion of treated soil. **Intermediate-term exposure**: for the adult, d_5 = a mean value (10% DFR= 0.71) based on 14 days with a 10% decrease each day after the day of application (day 0).; **for toddlers**,d_6 = a mean value (10% DFR) based on 14 days with a 10% decrease each day after day 0 + ingestion of treated soil (application rate on Day o). **Note**: Ingestion of treated soil times 6 months of application exposure, this is a very conservative estimate due to lost of pesticide through rain fall dilution, soil erosion, etc.. **Exposure from treated soil only = 3.15X10^{-5} mg/kg/day X 2 applications/month X 6 months= 3.8X10^{-4} mg/kg/day; MOE= 10 mg/kg/day/3.8X10^{-4} mg/kg/day = 26,000.**

e The upper percentile dermal transfer coefficient is assumed to be 43,000 cm^2/hr for adults (default, tier I) and 8,700 cm^2/hr for toddlers (default, tier I).

4. From Cumulative Exposure To Substances with a Common Mechanism of Toxicity

Myclobutanil is a member of the triazole class of systemic fungicides (*The Pesticide Book, 4th ed., 1994*). Other triazoles include bitertanol, cyproconazole, diclobutrazole, difenoconazole, diniconazole, fenbuconazole, flusilazole, hexaconazole, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, and triadimenol.

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information

in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

EPA does not have, at this time, available data to determine whether myclobutanil has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of these tolerance actions, therefore, EPA has not assumed that myclobutanil has a common mechanism of toxicity with other substances.

DETERMINATION OF SAFETY FOR U.S. POPULATION

1. *Acute Aggregate Risk*

   This risk assessment is not required as the HIARC did not identify any acute dietary risk endpoints.

2. *Chronic Aggregate Risk*

   Chronic Aggregate Exposure and Risk. Using the partially refined exposure assumptions described above, HED has concluded that aggregate exposure (food, water, and residential) to myclobutanil will not exceed HED's level of concern. For the U.S. population, 24% of the RfD is occupied by dietary (food) exposure. The estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for myclobutanil in drinking water as a contribution to chronic aggregate exposure. Therefore, OPP concludes with reasonable certainty that residues of myclobutanil in drinking water do not contribute significantly to the aggregate chronic human health risk at the present time considering the present uses and uses proposed in this action. HED has determined that the outdoor registered uses of myclobutanil would not fall under a chronic exposure scenario. HED concludes that there is a reasonable certainty that no harm will result from aggregate chronic exposure to myclobutanil residues.

3. *Short- and Intermediate-Term Aggregate Risk*

   The short-term NOEL for dermal exposure is based on a dermal exposure toxicity study. Since the NOEL is based on a dermal study, oral exposures generally cannot be used

directly to calculate a short-term aggregate exposure. However, as the HIARC determined that a dermal absorption factor of 100% should be used for risk assessment, oral exposures need not be multiplied by a modifying factor (converted to dermal equivalents) so that they can be compared to the dermal endpoint.

The chronic dietary exposure and calculated dietary MOE is shown below for the U.S. Population.

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE
U.S. Population (48 states)	0.005978	17000

Calculations:

$$Dietary\ MOE = \frac{Short\text{-}term\ NOEL}{Chronic\ dietary\ exposure}$$

$$= \frac{100\ mg/kg/day}{0.005978\ mg/kg/day} = 17{,}000$$

The dermal residential exposure for different scenarios and aggregate short-term MOEs is shown below for the U.S. Population (48 states).

Exposure scenario	Calculated Dietary MOE (from DEEM)	Total Residential Exposure (from Table 1) (mg/kg/day)	Total Residential MOE	Total Short-term MOE (Dietary + Residential)
Load/Apply Soluble Concentrate Using Low Pressure Handwand	17000 17000	1.0 1.9[a]	100 53[a]	99 52[a]
Load/Apply Soluble Concentrate Using Backpack	17000	0.49	200	200
Load/Apply Soluble Concentrate Using Garden Hose End Sprayer	17000	0.62	160	160

[a] Worst case day (based on label) of potential exposures = mixer/loader, + application (of lawn +roses + tree + flowers), and + Post-application exposure on day of application.

Calculations:

$$Residential\ MOE = \frac{Short\text{-}term\ NOEL}{Total\ residential\ exposure}$$

$$Load/Apply_{handwand} = \frac{100\ mg/kg/day}{1\ mg/kg/day} = 100$$

$$Load/Apply_{handwand} = \frac{100\ mg/kg/day}{1.9\ mg/kg/day} = 53$$

$$Load/Apply_{backpack} = \frac{100\ mg/kg/day}{0.49\ mg/kg/day} = 200$$

$$Load/Apply_{sprayer} = \frac{100\ mg/kg/day}{0.62\ mg/kg/day} = 160$$

$$Total\ MOE = \frac{1}{\frac{1}{MOE_{food}} + \frac{1}{MOE_{residential}}}$$

$$Total\ MOE_{Using\ Handwand} = \frac{1}{\frac{1}{17000} + \frac{1}{100}} = 99$$

$$Total\ MOE_{Using\ Handwand} = \frac{1}{\frac{1}{17000} + \frac{1}{53}} = 52$$

$$Total\ MOE_{Using\ Backpack} = \frac{1}{\frac{1}{17000} + \frac{1}{200}} = 200$$

$$Total\ MOE_{Using\ Sprayer} = \frac{1}{\frac{1}{17000} + \frac{1}{160}} = 160$$

There is a potential for short-term exposure from drinking water. However, as estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for drinking water as a contribution to chronic aggregate and acute aggregate exposures, contribution to short-term exposure should not exceed OPP's levels of concern either.

RAB1 concludes that short-term aggregate MOEs for adults are acceptable considering the default assumptions used in the derivation of exposure estimates and the fact that a LOEL was not identified in the 28-day rat dermal toxicity study [the HDT was the NOEL in this study] used to determine the MOE. **Chemical-specific dissipation data and residential use/usage information are required to further refine these post-application exposure estimates.**

4. *Intermediate-Term Aggregate Risk*

Intermediate-term exposure scenarios are present for adults during post-application activities.

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE
U.S. Population (48 states)	0.005978	1700

Calculations:

$$Dietary\ MOE = \frac{Intermediate\text{-}term\ NOEL}{Chronic\ dietary\ exposure}$$

$$= \frac{10\ mg/kg/day}{0.005978\ mg/kg/day} = 1700$$

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE	Post-Application MOE (from Table 3)	Total MOE
U.S. Population (48 states)	0.005978	1700	250	220

Calculations:

$$Total\ MOE = \frac{1}{\frac{1}{MOE_{food}} + \frac{1}{MOE_{residential}}}$$

$$Total\ intermediate\text{-}term\ MOE = \frac{1}{\frac{1}{1700} + \frac{1}{250}} = 220$$

There is a potential for intermediate-term exposure from drinking water. However, as estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for drinking water as a contribution to chronic aggregate and acute aggregate exposures, contribution to intermediate-term exposure should not exceed OPP's levels of concern either.

DETERMINATION OF CANCER RISK

A cancer risk assessment is not needed since myclobutanil is classified as Category E: not carcinogenic in two acceptable animal studies.

ENDOCRINE DISRUPTOR EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

Based on the adverse testicular findings, and increase in the number of stillborns, and a decrease in pup weight gain during lactation, in the chronic toxicity and reproduction studies in rats, myclobutanil should be considered as a candidate for evaluation as an endocrine disruptor.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

In assessing the potential for additional sensitivity of infants and children to residues of myclobutanil, HED considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproductive toxicity study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing fetus resulting from maternal pesticide exposure during gestation. Reproductive toxicity studies provide information relating to pre- and post-natal effects from exposure to the pesticide, information on the reproductive capability of mating animals, and data on systemic toxicity.

EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty factor/margin of exposure (safety) is designed to account for inter-species extrapolation and intra-species variability. Under the Food Quality Protection Act (FQPA), P.L. 104-170, which was promulgated in 1996 as an amendment to the Federal Food, Drug and Cosmetic Act (FFDCA), the Agency was directed to "ensure that there is a reasonable certainty that no harm will result to infants and children" from aggregate exposure to a pesticide chemical residue. The law further states that in the case of threshold effects, for purposes of providing this reasonable certainty of no harm, "an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide residue only if, on the basis of reliable data, such margin will be safe for infants and children."

1. *Developmental Toxicity Studies*

   a. Rats. In the developmental study (MRID# 00141672)in rats, the maternal (systemic) NOEL was 93.8 mg/kg/day, based on rough hair coat, and salivation at the LOEL of 312.6 mg/kg/day. The developmental (fetal) NOEL was 93.8 mg/kg/day based on incidences of 14th rudimentary and 7th cervical ribs at the LOEL of 312.6 mg/kg/day.

   b. Rabbits. In the developmental toxicity study (MRID# 00164971) in rabbits, the

maternal (systemic) NOEL was 60 mg/kg/day, based on reduced weight gain, clinical signs of toxicity and abortions at the LOEL of 200 mg/kg/day. The developmental (fetal) NOEL was 60 mg/kg/day, based on increases in number of resorptions, decreases in litter size, and a decrease in the viability index at the LOEL of 200 mg/kg/day.

2. *Reproductive Toxicity Studies*

Rats. In the 2-generation reproductive toxicity study (MRID# 00143766, 00149581) in rats, the parental (systemic) NOEL was 2.5 mg/kg/day, based on increased liver weights and liver cell hypertrophy at the LOEL of 10 mg/kg/day. The developmental (pup) NOEL was 10 mg/kg/day, based on decreased pup body weight during lactation at the LOEL of 50 mg/kg/day. The reproductive (pup) NOEL was 10 mg/kg/day, based on the increased incidence of stillborns, and atrophy of the testes, epididymides, and prostate at the LEL of 50 mg/kg/day.

3. *Pre- and Post-Natal Sensitivity*

The pre- and post-natal toxicology data base for myclobutanil is complete with respect to current toxicological data requirements. Based on the developmental and reproductive toxicity studies discussed above, for myclobutanil there does not appear to be an extra sensitivity for pre- or post-natal effects.

Based on the above, HED concludes that reliable data support use of a 100-fold margin of exposure/uncertainty factor, rather than the standard 1000-fold margin/factor, to protect infants and children.

4. *Acute Aggregate Risk for Infants and Children*

This risk assessment is not required as the HIARC did not recommend an acute dietary risk endpoint.

5. *Chronic Aggregate Risk for Infants and Children*

Using the partially refined exposure assumptions described above, HED has concluded that the percent of the RfD that will be utilized by dietary (food only) exposure to residues of myclobutanil ranges from 24% for nursing infants (<1 year old) up to 73% for children (1-6 years old). Despite the potential for exposure to myclobutanil in drinking water, HED does not expect the chronic aggregate exposure to exceed 100% of the RfD. HED concludes that there is a reasonable certainty that no harm will result to infants and children from chronic aggregate exposure to myclobutanil residues.

6. *Short-Term Aggregate Risk for Infants and Children*

The short-term NOEL for dermal exposure is based on a dermal exposure toxicity study. Since the NOEL is based on a dermal study, oral exposures generally cannot be used directly to calculate a short-term aggregate exposure. However, as the HIARC determined that a dermal absorption factor of 100% should be used for risk assessment, oral exposures need not be multiplied by a modifying factor (converted to dermal equivalents) so that they can be compared to the dermal endpoint.

The chronic dietary exposure and calculated dietary MOE is shown below for children (1-6

years old):

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE
children (1-6 years old)	0.018265	5500

Calculations:

$$Dietary\ MOE = \frac{Short\text{-}term\ NOEL}{Chronic\ dietary\ exposure}$$

$$= \frac{100\ mg/kg/day}{0.018265\ mg/kg/day} = 5{,}500$$

The dermal residential exposure is 0.85 mg/kg/day (reentry). The calculated dietary MOE for children (1-6 years old) is 5,500.

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE	Post-Application MOE (from Table 3)	Total MOE
children (1-6 years old)	0.018265	5500	120	120

For the short-term aggregate risk of the most highly exposed subgroup (children (1-6 years old)), the calculated MOE is 120. There is a potential for short-term exposure from drinking water. However, as estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for drinking water as a contribution to chronic aggregate and acute aggregate exposures, contribution to short-term exposure should not exceed OPP's levels of concern either. RABI concludes that short-term aggregate MOEs for children (1-6 years old) are acceptable.

Calculations:

$$Total\ MOE = \frac{1}{\frac{1}{MOE_{food}} + \frac{1}{MOE_{residential}}}$$

$$Total\ short\text{-}term\ MOE = \frac{1}{\frac{1}{5{,}500} + \frac{1}{120}} = 120$$

There is a potential for short-term exposure from drinking water. However, as estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for drinking water as a contribution to chronic aggregate and acute aggregate exposures, contribution to short-term exposure should not exceed OPP's levels

of concern either.

RABI concludes that short-term aggregate MOEs for adults are acceptable considering the default assumptions used in the derivation of exposure estimates and the fact that a LOEL was not identified in the 28-day rat dermal toxicity study [the HDT was the NOEL in this study] used to determine the MOE. **Chemical-specific dissipation data and residential use/usage information are required to further refine these post-application exposure estimates.**

7. *Intermediate-Term Aggregate Risk for Infants and Children*

The intermediate-term NOEL for dermal exposure is based on an oral exposure toxicity study. The HIARC determined that a dermal absorption factor of 100% should be used for this risk assessment.

The chronic dietary exposure from myclobutanil is 0.018265 mg/kg/day. The calculated myclobutanil dietary MOE for children (1-6 years old) is 530.

Subgroup	Exposure (from DEEM) (mg/kg/day)	Calculated Dietary MOE
children (1-6 years old)	0.018265	550

Calculations:

$$Dietary\ MOE = \frac{Intermediate\text{-}term\ NOEL}{Chronic\ dietary\ exposure} \quad (12)$$

$$= \frac{10\ mg/kg/day}{0.018265\ mg/kg/day} = 550$$

Subgroup	ARC (from DRES) (mg/kg/day)	Calculated Dietary MOE (from DRES)	Post-Application MOE (from Table 3)	Total MOE
children (1-6 years old)	0.018265	550	160	120

The dermal residential exposure is 0.061 mg/kg/day. The calculated intermediate-term residential MOE for children (1-6 years old) is 160.

Calculations:

$$Residential\ MOE = \frac{Intermediate\text{-}term\ NOEL}{Residential\ exposure}$$

$$= \frac{10\ mg/kg/day}{0.061\ mg/kg/day} = 160$$

For the intermediate-term aggregate risk of the most highly exposed subgroup (children (1-6 years old)), the calculated MOE is 120.

Calculations:

$$Total\ MOE = \frac{1}{\frac{1}{MOE_{food}} + \frac{1}{MOE_{residential}}}$$

$$Total\ intermediate\text{-}term\ MOE = \frac{1}{\frac{1}{550} + \frac{1}{160}} = 120$$

There is a potential for intermediate-term exposure from drinking water. However, as estimated average concentrations of myclobutanil in surface and ground water are less than OPP's levels of concern for drinking water as a contribution to chronic aggregate and acute aggregate exposures, contribution to intermediate-term exposure should not exceed OPP's levels of concern either.

DETERMINATION OF SAFETY TO OCCUPATIONALLY EXPOSED WORKERS

1. Acute data for this formulation were available to RAB1 in conjunction with a recent import tolerance petition for bananas (PP#2E04141). The proposed work clothing and personal protective equipment (PPE) appearing on the label for Rally 40W in water-soluble pouches include long-sleeved shirt and long pants, waterproof gloves, shoes plus socks, protective eyewear and chemical-resistant headgear for overhead exposure; These work clothing and PPE are in compliance with the Worker Protection Standard(WPS).
2. Acute data for the technical are also available to RAB1. According to the recent import tolerance petition for bananas (PP#2E04141), myclobutanil is a category III for acute oral and acute dermal; category IV for primary dermal irritation and acute inhalation; ***and category I for primary eye irritation***. Based on these values, the **Human Hazard Signal Word, should be DANGER** and the **restricted entry interval (REI) should be 48 hours to be in compliance with the WPS**. The registrant's label has a human hazard signal word of **WARNING**, and a **REI of 24 hours**; therefore the **label is not in compliance**. Additional data may have been submitted to support a human hazard signal word of WARNING, and a 24 hour REI for this chemical. **RD should insure that the appropriate Human Hazard Signal Word, and the REI statement appears on the label.**

3. Occupational exposure assumptions and estimates are summarized in Tables 1 and 2, respectively.

   Worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED) and/or the PHED Surrogate Exposure Guide (May 1997) with the worker wearing a single layer of clothing plus gloves **(note: two flagger scenarios (when there is no mechanical flagger utilized) were addressed; 1) is assumed to wear no clothing, and 2) single layer clothing with no gloves)** for myclobutanil in water-soluble pouches.

4. Using these exposure assumptions, HED has concluded that the dermal MOEs that will result from the handling and application of myclobutanil by workers utilizing aerial and ground equipment, are the following ranges : *For short-term* -**aerial,** for mixer/loader is 2,900 (for inhalation is > 2,900) to 5,600 (for inhalation is >5,600) for applicator; **flagger**, for scenario 1) is 560 and 2) is 2,600 (for inhalation is >2,600); and **groundboom**, for mixer/loader is 12,000 (for inhalation is >12,000) to 8,300 (for inhalation is >8,300) for applicator. *For intermediate-term* -**aerial**, for mixer/loader is 290 (for inhalation is > 2,900) to 560 (for inhalation is >2,900) for applicator; **flagger,** for scenario 1) is 56 and 2) is 260 (for inhalation is >2,600); and **groundboom**, for mixer/loader is 1,200 (for inhalation is >1,200) to 830 (for inhalation is >1,200) for applicator. These MOEs do not exceed HED's level of concern, **except for the intermediate-term flagger scenario #1 (no clothing)**, for occupationally exposed workers.

OTHER CONSIDERATIONS

Metabolism in Plants

1. The nature of the residue in plants is adequately understood. The residue of concern is myclobutanil plus its alcohol metabolite (free and bound), as specified in 40 CFR 180.443(a).

Analytical Enforcement Methodology

2. An adequate enforcement method (Rohm and Haas Method 34S-88-10, MRID# 408033-02) is available to enforce the established tolerances. Quantitation is by GLC using an Nitrogen/Phosphorus detector for myclobutanil and an Electron Capture detector (Ni^{63}) for residues measured as the alcohol metabolite. A copy of this method is on file in PP#4E4302.

Magnitude of the Residues

3. Residues of myclobutanil and its alcohol metabolite are not expected to exceed 1.0 ppm in/on artichokes as a result of this Section 18 use. **A time-limited tolerance for the combined residues of myclobutanil and its alcohol metabolite (free and bound) should be established at this level.**

Magnitude of the Residues (Meat/Milk/Poultry and Eggs)

4. Secondary residues are not expected in animal commodities as no feedstuffs are **associated** with these Section 18 uses. Meat/milk/poultry/egg tolerances have been established as a result of other myclobutanil uses.

Rotational Crop Restrictions

5. As artichokes are normally not rotated, issues pertaining to rotational crops are not applicable to this petition.

International Residue Limits

6. There are no Codex, Canadian or Mexican residue limits established for myclobutanil and its metabolites on the commodities included in these Section 18 requests. Thus, harmonization is not an issue for these Section 18 actions.

SUPPLEMENTAL INFORMATION

Occupational Exposure

Table 1. Occupational Exposure Assumptions

PARAMETER	ASSUMPTION
Pesticide Handlers Exposure Database (PHED), Version 1.1, Surrogate Exposure Guide (May 1997)	Mixer/Loader (wettable powder, water soluble bags, single layer clothing plus gloves): Dermal = 9.8 µg/lb ai handled (for inhalation = 0.11 µg/lb). *Low Confidence Run.*
	Applicator - Ground (ground boom, open cab, single layer clothing plus gloves): Dermal = 14.0 µg/lb ai applied (for inhalation = 0.74 µg/*lb; High-Confidence Run*). *Medium Confidence Run.*
	Applicator - Air (liquid formulations, enclosed cockpit, single layer clothing, no gloves): Dermal = 5.0 µg/lb ai applied (for inhalation = 0.07 µg/lb; *Medium Confidence Run*). *Low Confidence Run.*
	Flagger - Air (no clothing):Dermal = 53.0 µg/lb ai handled (for inhalation = 0.35 µg/*lb; High Confidence Run*). *Medium Confidence Run.* Flagger - Air (single layer clothing, no gloves):Dermal = 11.0 µg/lb ai handled *High Confidence Run.*
Percent Absorption	Dermal:100% should be used for risk assessments because 1) a dermal absorption study was not available and 2) a dermal absorption factor could not be estimated due to the lack of comparative NOELs/LOELs from oral and dermal toxicity studies in the same species.
Application Type	Ground or aerial
Minimum Finish Spray	Ground: 75 gal/A (estimated minimum dilution rate) Air: 5 gal/A (dilution rate for artichokes)
Maximum Application Rate	0.6 lb ai/A/season
Acres Treated/Day (default values)	Ground: 88 acres Air: 350 acres
For California (Artichokes) average.	Based on section 18 of 7,000 Acres (maximum) statewide.

PARAMETER	ASSUMPTION
Worker Weight	60 kg (based on Tox endpoint)
Number of Farms Treated by PCO (Professional Chemical Operator)	To treat 7,000 acres: Ground: 80 days; Air: 20 days. Several operators.

Table 2. Occupational Exposure and Risk Assessment[a]

Worker	Average Daily Dermal Dose[b] (mg/kg/day)	Short-Term Dermal MOE[c]	Intermediate-Term Dermal MOE[d]
Ground Mixer/Loader	$8.6X10^{-3}$ ($9.7X10^{-5}$)[e]	12,000 (>12,000)[f]	1,200 (>1,200)[f]
Ground Applicator	$1.2X10^{-2}$ ($6.5X10^{-4}$)[e]	8,300 (>8,300)[f]	830 (>1,200)[f]
Aerial Mixer/Loader	$3.4X10^{-2}$ ($3.8X10^{-4}$)[e]	2,900 (>2,900)[f]	290 (>2,900)[f]
Aerial Applicator	$1.8X10^{-2}$ ($2.4X10^{-4}$)[e]	5,600 (>5,600)[f]	560 (>2,900)[f]
Flagger	$1.8X10^{-1}$ ($1.2X10^{-3}$)[e] *($3.8X10^{-2}$)*[g]	560 (>2,600)[f] *(2,600)*[g]	56 (>2,600)[f] *(260)*[g]

[a] MOEs are expressed to two significant figures.

[b] Average Daily Dermal Dose (ADD) = PHED unit exposure in mg x % absorption x application rate x acres treated/day ÷ kg body weight.

[c] Short-Term Occupational Dermal Exposure MOE = NOEL/ADD (where NOEL = 100 mg/kg/day).

[d] Intermediate-Term Occupational Dermal Exposure MOE = NOEL/ADD (where NOEL = 10 mg/kg/day).

[e] Average Daily Inhalation Dose (ADD) = PHED inhalation unit exposure in mg x % absorption x application rate x acres treated/day ÷ kg body weight.

[f] Inhalation Occupational Exposure MOE = NOEL/ADD (where NOEL = 10 mg/kg/day).

[g] Flagger wearing single layer of clothing, no gloves: Average Daily Dermal Dose (ADD) = PHED unit exposure in mg x % absorption x application rate x acres treated/day ÷ kg body weight.

Dietary Exposure

Table 3. Residue Consideration Summary Table

PARAMETER	PROPOSED USE	RESIDUE DATA
CHEMICAL	Myclobutanil	Myclobutanil
FORMULATION	Rally ® 40W Fungicide in Water-Soluble Pouches (Rohm and Haas, EPA Reg. No. 707-215)	NOVA ® 40W Fungicide in Water-Soluble Pouches (Rohm and Haas, EPA Reg. No. 707-221)
CROP	Artichokes	Artichokes
TYPE APPLICATION	Aerial or Ground	not specified
# APPLICATIONS	6 applications	1-6 applications
TIMING	max of 3 in 14 days	not specified
RATE/APPLICATION	4 ounces product/A 0.1 lbs ai/A	0.07-0.12 lbs ai/A
RATE/YEAR or SEASON	24 ounces product/A/crop 0.6 lbs ai/A/crop	0.12-0.60 lbs ai/A/crop
MAXIMUM RESIDUE	N/A	0.75 ppm at 0-day PHI
RESTRICTIONS	5-day PHI	3-day PHI
RESIDUE DATA SOURCE	N/A	Summary of 4 trials conducted in Spain and Italy, 1990-97
PERFORMING LAB	N/A	Rohm & Haas

Additional Information

Progress Toward Registration.

This is **the first** §18 request for this use in the state of CA.

Reregistration Status.

Myclobutanil is not a FIFRA '88 reregistration active ingredient.

Attachments: Chronic Dietary Exposure Analysis (7/13/98)

cc with Attachments: J. Cruz (RAB1), G. Kramer (RAB1)
RDI: M. Morrow (7/31/98), Team (7/16/98)
G. Kramer: CM#2:(703)305-5079:7509C:RAB1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: July 13, 1998

SUBJECT: Myclobutanil - Chronic Dietary Exposure Analysis. Chemical#: 128857. Caswell#: 723K. DP Barcode: D247290.

FROM: Susie Chun, Chemist
Registration Action Branch 1 (RAB1)
HED (7509C)

THROUGH: Melba Morrow, D.V.M., Branch Senior Scientist
RAB1
HED (7509C)

TO: George F. Kramer, Ph.D., Chemist
RAB1
HED (7509C)

Action Requested

Provide an estimate of the chronic dietary exposure and associated risk for myclobutanil resulting from published tolerances, pending tolerances, percent crop treated, and the proposed Section 18 tolerance level of 1.0 ppm on globe artichokes. A previous chronic dietary exposure analysis incorporating published and pending tolerances, percent crop treated where available, proposed tolerances, anticipated residues for bananas only was completed on 6/18/98.

Toxicological Endpoint

The reference Dose (RfD) used is 0.025 mg/kg/day. The Hazard Identification Assessment Review Committee (HIARC) selected a NOEL of 2.49 mg/kg/day based on testicular atrophy at 9.94 mg/kg/day (LOEL) in the Two-Generation reproduction study in rats. An uncertainty factor of 100 was chosen; the resulting RfD for use in the chronic dietary exposure is 0.025 mg/kg/day (Memo, J. Rowland, 11/3/97). For acute dietary risk assessment, the HIARC did not recommend an acute dietary endpoint. The Committee determined that the **10 x** factor to account for enhanced sensitivity of infants and children (as required by FQPA) should be removed. This decision was confirmed by the *ad hoc* FQPA Safety Factor Committee (R. Keigwin and W. Burnam, personal communication).

Residue Information

Tolerances for myclobutanil (including Time-Limited Tolerances) are published in 40 CFR §180.443. For this analysis, tolerance level residues and 100% crop treated (%CT) information where were used for the proposed commodity of artichokes. Percent CT (personal communication from BEAD, A. Halvorson, 6/7/98) information was used on other raw agricultural commodities (RACs) included in this analysis.

Results

The Dietary Exposure Evaluation Model (DEEM™) analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-91 nationwide Continuing Surveys for Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The chronic DEEM™ used mean consumption (3 day average) and gave the following results:

Subgroups	Exposure (mg/kg/day)	% RfD
U.S. Population (48 states)	0.005978	23.9
Non-Hispanic other than black or white	0.007454	29.8
All infants (< 1 year)	0.013618	54.5
Nursing Infants (< 1 year old)	0.005964	23.9
Non-Nursing Infants (< 1 year old)	0.016840	67.4
Children (1-6 years old)	0.018265	73.1
Children (7-12 years old)	0.008602	34.4
Females (13+/nursing)	0.007627	30.5

The results of this analysis indicate that the chronic dietary risk associated with existing uses and the proposed use of myclobutanil on artichokes is below the Agency's level of concern.

Attachment 1: Residue File
Attachment 2: Chronic DEEM™ analysis (S. Chun, 7/10/98)

cc: S. Chun (RAB1); B. Steinwand (CEB1), 98CA0029
RDI: DRES Team (7/10/98)
S. Chun:811-Bay:CM#2:(703)305-2249:7509C:RAB1

Attachment 1

FILENAME: C:\deem89\resdata\128857.r91

CHEMICAL NAME: Myclobutanil

RfD(CHRONIC): .025000 mg/kg/DAY NOEL(CHRONIC): .000000 mg/kg/day

RfD(ACUTE): .000000 mg/kg/DAY NOEL(ACUTE): .000000 mg/kg/day Q*=.0000

Date created/last modified: 07-10-1998/10:14:17/8 Program ver 6.16

Comment: C. Kramer, 98CA0029, Section 18 for artichokes

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
040	R	ALMONDS	000.100000		01.000	00.010	0F3876
377	L	APPLES-JUICE-CONCENTRATE	000.500000		03.900	00.600	7F3476
053	L	APPLES-DRIED	000.500000		08.000	00.600	7F3476
054	L	APPLES-JUICE/CIDER	000.500000		01.300	00.600	7F3476
052	L	APPLES	000.500000		01.000	00.600	7F3476
410	M	APRICOT JUICE	002.000000		01.000	00.010	1F3954
060	M	APRICOTS-DRIED	002.000000		06.000	00.010	1F3954
059	M	APRICOTS	002.000000		01.000	00.010	1F3954
181	A	ARTICHOKES-GLOBE	001.000000		01.000	01.000	98CA0029, S18, New
260	A	ASPARAGUS	000.020000		01.000	01.000	98MI001, S18, Pending
497	L	BALSAM PEAR	000.500000		01.000	00.080	9F3812, Pending
073	A	BANANAS-DRIED	004.000000		03.900	01.000	2E04141
378	A	BANANAS-JUICE	004.000000		01.000	01.000	2E04141
072	A	BANANAS	004.000000		01.000	01.000	2E04141
324	U	BEEF-FAT W/O BONES	000.050000		01.000	01.000	03F3876
325	U	BEEF-KIDNEY	000.200000		01.000	01.000	03F3876
326	U	BEEF-LIVER	001.000000		01.000	01.000	03F3876
327	U	BEEF-LEAN(FAT/FREE)W/O BONES	000.100000		01.000	01.000	03F3876
322	U	BEEF-OTHER ORGAN MEATS	000.200000		01.000	01.000	03F3876
323	U	BEEF-DRIED	000.100000		01.920	01.000	03F3876
321	U	BEEF-MEAT BYPRODUCTS	000.200000		01.000	01.000	03F3876
152	J	BITTER MELON	000.300000		01.000	01.000	96CA0038, S18, EXP 11/30/98
380	N	BLACKBERRIES-JUICE	001.000000		01.000	01.000	98OR023, Pending
001	N	BLACKBERRIES	001.000000		01.000	01.000	98OR023, Pending
143	J	CASABAS	000.300000		01.000	01.000	96CA0038, S18, EXP 11/30/98
062	M	CHERRIES-DRIED	005.000000		04.000	00.470	2F4116
063	M	CHERRIES-JUICE	005.000000		01.500	00.470	2F4116
061	M	CHERRIES	005.000000		01.000	00.470	2F4116
368	V	CHICKEN FAT W/O BONES	000.020000		01.000	01.000	7F3476
369	V	CHICKEN-LEAN/FATFREE W/O BONE	000.020000		01.000	01.000	7F3476
367	V	CHICKEN-GIBLETS(LIVER)	000.020000		01.000	01.000	7F3476
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	000.020000		01.000	01.000	7F3476
366	V	CHICKEN-BYPRODUCTS	000.020000		01.000	01.000	7F3476
386	J	CHRISTOPHINE	000.300000		01.000	01.000	96CA0038, S18, EXP 11/30/98
290	A	COTTONSEED-OIL	000.020000		01.000	00.010	4F4317
291	A	COTTONSEED-MEAL	000.020000		01.000	00.010	4F4317

055	L	CRABAPPLES	000.500000	01.000	01.000	9F3812, Pending
144	J	CRENSHAWS	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
148	J	CUCUMBERS	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
365	X	EGGS-YOLK ONLY	000.020000	01.000	01.000	7F3476
363	X	EGGS-WHOLE	000.020000	01.000	01.000	7F3476
364	X	EGGS-WHITE ONLY	000.020000	01.000	01.000	7F3476
332	U	GOAT-LIVER	001.000000	01.000	01.000	03F3876
329	U	GOAT-OTHER ORGAN MEATS	000.200000	01.000	01.000	03F3876
333	U	GOAT-LEAN (FAT/FREE) W/O BONE	000.100000	01.000	01.000	03F3876
331	U	GOAT-KIDNEY	000.200000	01.000	01.000	03F3876
328	U	GOAT-MEAT BYPRODUCTS	000.200000	01.000	01.000	03F3876
330	U	GOAT-FAT W/O BONE	000.050000	01.000	01.000	03F3876
392	A	GRAPES-JUICE-CONCENTRATE	001.000000	03.600	00.790	7F3476
315	A	GRAPES-WINE AND SHERRY	001.000000	01.000	00.790	7F3476
195	A	GRAPES-LEAVES	001.000000	01.000	00.790	7F3476
015	A	GRAPES-JUICE	001.000000	01.200	00.790	7F3476
014	A	GRAPES-RAISINS	010.000000	04.300	00.790	7H5524
013	A	GRAPES	001.000000	01.000	00.790	7F3476
125	A	HOPS	005.000000	01.000	01.000	98WA0006, Pending
334	U	HORSEMEAT	000.100000	01.000	01.000	03F3876
004	N	LOGANBERRIES	001.000000	01.000	01.000	98OR023, Pending
146	J	MELONS-PERSIAN	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
145	J	MELONS-HONEYDEW	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
141	J	MELONS-CANTALOUPES-JUICE	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
142	J	MELONS-CANTALOUPES-PULP	000.300000	01.000	01.000	96CA0038, S18, EXP 11/30/98
319	X	MILK-FAT SOLIDS	000.200000	01.000	01.000	0F3876
398	X	MILK-BASED WATER	000.200000	01.000	01.000	0F3876
320	X	MILK SUGAR (LACTOSE)	000.200000	01.000	01.000	0F3876
318	X	MILK-NONFAT SOLIDS	000.200000	01.000	01.000	0F3876
064	M	NECTARINES	002.000000	01.000	00.210	9F3811
066	M	PEACHES-DRIED	002.000000	07.000	00.220	9F3811
402	M	PEACHES-JUICE	002.000000	01.000	00.220	9F3811
065	M	PEACHES	002.000000	01.000	00.220	9F3811
404	L	PEARS-JUICE	000.500000	01.000	00.080	9F3812, Pending
057	L	PEARS-DRIED	000.500000	06.250	00.080	9F3812, Pending
056	L	PEARS	000.500000	01.000	00.080	9F3812, Pending
311	A	PEPPERMINT-OIL	002.500000	01.000	01.000	98WA0002, 98ID0011, 98MT0010, SECT 18, PENDING
310	A	PEPPERMINT	002.500000	01.000	01.000	98WA0002, 98ID0011, 98MT0010, SECT 18, PENDING
156	I	PEPPERS-CHILLI INCL JALAPENO	001.000000	01.000	01.000	98NM0004, S18,Pending
157	I	PEPPERS-OTHER	001.000000	01.000	01.000	98NM0004, S18,Pending
155	I	PEPPERS-SWEET(GARDEN)	001.000000	01.000	01.000	98NM0004, S18,Pending
158	I	PIMIENTOS	001.000000	01.000	01.000	98NM0004, S18,Pending
094	A	PLANTAINS-RIPE	004.000000	01.000	01.000	2E04141
481	A	PLANTAINS-DRIED	004.000000	03.900	01.000	2E04141
480	A	PLANTAINS-GREEN	004.000000	01.000	01.000	2E04141
068	M	PLUMS-PRUNES(DRIED)	008.000000	05.000	00.030	1F3954
069	M	PLUMS/PRUNE-JUICE	002.000000	01.400	00.030	1F3954
067	M	PLUMS(DAMSONS)	002.000000	01.000	00.030	1F3954
347	U	PORK-LEAN (FAT FREE) W/O BONE	000.100000	01.000	01.000	03F3876

346	U	PORK-LIVER	001.000000	01.000	01.000 03F3876
345	U	PORK-KIDNEY	000.200000	01.000	01.000 03F3876
344	U	PORK-FAT W/O BONE	000.050000	01.000	01.000 03F3876
343	U	PORK- OTHER ORGAN MEATS	000.200000	01.000	01.000 03F3876
342	U	PORK-MEAT BYPRODUCTS	000.200000	01.000	01.000 03F3876
362	V	POULTRY-OTHER-FAT W/O BONES	000.020000	01.000	01.000 7F3476
360	V	POULTRY-OTHER-LEAN (FAT FREE)	000.020000	01.000	01.000 7F3476
361	V	POULTRY-OTHER-GIBLETS(LIVER)	000.020000	01.000	01.000 7F3476
149	J	PUMPKIN	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98
058	L	QUINCES	000.500000	01.000	01.000 9F3812, Pending
005	N	RASPBERRIES	001.000000	01.000	01.000 98OR023, Pending
338	U	SHEEP-FAT W/O BONE	000.050000	01.000	01.000 03F3876
337	U	SHEEP-OTHER ORGAN MEATS	000.200000	01.000	01.000 03F3876
336	U	SHEEP-MEAT BYPRODUCTS	000.200000	01.000	01.000 03F3876
339	U	SHEEP-KIDNEY	000.200000	01.000	01.000 03F3876
340	U	SHEEP-LIVER	001.000000	01.000	01.000 03F3876
341	U	SHEEP-LEAN (FAT FREE)W/O BONE	000.100000	01.000	01.000 03F3876
313	A	SPEARMINT-OIL	002.500000	01.000	01.000 98WA0002, 98ID0011, 98MT0010, SECT 18, PENDING
312	A	SPEARMINT	002.500000	01.000	01.000 98WA0002, 98ID0011, 98MT0010, SECT 18, PENDING
415	J	SQUASH-SPAGHETTI	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98
151	J	SQUASH-WINTER	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98
150	J	SQUASH-SUMMER	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98
416	A	STRAWBERRIES-JUICE	000.500000	01.000	01.000 98FL0002, S18, EXP 3/31/99
017	A	STRAWBERRIES	000.500000	01.000	01.000 98FL0002, S18, EXP 3/31/99
159	I	TOMATOES-WHOLE	000.300000	01.000	01.000 97CA042, S18, EXP 7/28/98
423	I	TOMATOES-DRIED	000.300000	14.300	01.000 97CA042, S18, EXP 7/28/98
160	I	TOMATOES-JUICE	000.300000	01.500	01.000 97CA042, S18, EXP 7/28/98
162	I	TOMATOES-PASTE	001.200000	05.400	01.000 97CA042, S18, EXP 7/28/98
163	I	TOMATOES-CATSUP	000.600000	02.500	01.000 97CA042, S18, EXP 7/28/98
161	I	TOMATOES-PUREE	000.600000	03.300	01.000 97CA042, S18, EXP 7/28/98
153	J	TOWELGOURD	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98
357	V	TURKEY--FAT W/O BONES	000.020000	01.000	01.000 7F3476
356	V	TURKEY-GIBLETS (LIVER)	000.020000	01.000	01.000 7F3476
355	V	TURKEY-BYPRODUCTS	000.020000	01.000	01.000 7F3476
449	V	TURKEY-OTHER ORGAN MEATS	000.020000	01.000	01.000 7F3476
358	V	TURKEY-LEAN/FAT FREE W/O BONE	000.020000	01.000	01.000 7F3476
424	U	VEAL-FAT W/O BONES	000.050000	01.000	01.000 03F3876
425	U	VEAL-LEAN (FATFREE) W/O BONES	000.100000	01.000	01.000 03F3876
430	U	VEAL-MEAT BYPRODUCTS	000.200000	01.000	01.000 03F3876
426	U	VEAL-KIDNEY	000.200000	01.000	01.000 03F3876
427	U	VEAL-LIVER	001.000000	01.000	01.000 03F3876
428	U	VEAL-OTHER ORGAN MEATS	000.200000	01.000	01.000 03F3876
429	U	VEAL-DRIED	000.100000	01.920	01.000 03F3876
436	J	WATERMELON-JUICE	000.300000	01.000	01.000 98HI0002, S18, Pending
147	J	WATERMELON	000.300000	01.000	01.000 98HI0002, S18, Pending
439	J	WINTERMELON	000.300000	01.000	01.000 96CA0038, S18, EXP 11/30/98

Attachment 2: Chronic DEEM™ Analysis

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for MYCLOBUTANIL (1989-92 data)
Residue file name: 128857 Adjustment factor #2 used.
Analysis Date 07-10-1998 Residue file dated: 07-10-1998/10:14:17/8
Reference dose (RfD, CHRONIC) = 0.025000 mg/kg body-wt/day
COMMENT 1: G. Kramer, 98CA0029, Section 18 for artichokes

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Pop - 48 states - all seasons	0.005978	23.9%
U.S. Population - spring season	0.005826	23.3%
U.S. Population - summer season	0.005768	23.1%
U.S. Population - autumn season	0.006381	25.5%
U.S. Population - winter season	0.005930	23.7%
Northeast region	0.005979	23.9%
Midwest region	0.006034	24.1%
Southern region	0.005732	22.9%
Western region	0.006324	25.3%
Pacific Region	0.006267	25.1%
Hispanics	0.005868	23.5%
Non-hispanic whites	0.006094	24.4%
Non-hispanic blacks	0.005002	20.0%
Non-hispanic other than black or white	0.007454	29.8%
All infants (<1 year)	0.013618	54.5%
Nursing infants (<1 year)	0.005964	23.9%
Non-nursing infants (<1 year)	0.016840	67.4%
Children (1-6 years)	0.018265	73.1%
Children (7-12 years)	0.008602	34.4%
Females (13-19 yrs/not preg. or nursing)	0.004431	17.7%
Females (20+ years/not preg. or nursing)	0.004101	16.4%
Females (13-50 years)	0.003998	16.0%
Females (13+/pregnant/not nursing)	0.005042	20.2%
Females (13+/nursing)	0.007627	30.5%
Males (13-19 years)	0.005026	20.1%
Males (20+ years)	0.003813	15.3%
Seniors (55+)	0.004431	17.7%

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13544

R120632

Chemical: Myclobutanil

PC Code:
128857
HED File Code: 11100 Other Chemistry Documents
Memo Date: 8/4/1998
File ID: 00000000
Accession #: 412-06-0013

HED Records Reference Center
2/27/2006